PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	[illegible] 2005
Applicant's or agent's file reference 068911.0107	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US05/06216	26 February 2005 (26.02.2005)	27 February 2004 (27.02.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61 K 31/557, 31/12, 35/78 and US Cl.: 424/778; 514/690

Applicant

METAPROTEOMICS, LLC

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [X] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Sreeni Padmanabhan Telephone No. 571-272-0600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/06216

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-7	YES
	Claims NONE	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-7	NO
Industrial applicability (IA)	Claims 1-7	YES
	Claims NONE	NO

2. Citations and explanations:

The instant invention is drawn to a composition comprising a reduced isoalpha acid and isoalpha acid isolated from hops, and a method of reducing inflammation by administering said composition.

Claims 1-7 lack an inventive step under PCT Article 33(3) as being obvious over Kuhrts US 2002/0086070.

Kuhrts teaches a pharmaceutical composition comprising hops (Humulus lupus L) extract for treating inflammatory disorders such as osteoarthritis, rheumatoid arthritis. See column 2, paragraph [0014], [0016]. Kuhrts further teaches liquid carbon dioxide under supercritical conditions is a preferred extraction technique to obtain the components from the hops. See page 2, paragraphs [0016],and [0018]; page 6, claims 1-14.

Since Kuhrts teaches the same extract i.e., derived from hops obtained by the same process as recited by the instant claims and specification, Kuhrts hops extract will contain the components isoalpha acids and reduced isoalpha acids as recited by instant claims.

Kuhrts does not expressly teach the ratio of reduced isoalpha acid : isoalpha acid as about 3:1 to about 1:10 in the composition.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of the reduced isoalpha acid : isoalpha acid employed in the composition of Kuhrts, to obtain a desired effect such as reducing inflammation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of Iso-alpha acid and reduced isoalpha acid employed in the pharmaceutical compositions for methods of reducing inflammation in which the ratio of isoalpha acid : isoalpha acid is about 3:1 to about 1:10, since the optimization of effective amounts of known agents to be administered , is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Claim 7 lack an inventive step under PCT Article 33(3) as being obvious over Tobe et al. (5,604,263).

Tobe teaches a method of treating inflammatory disorder osteoporosis, comprising administering a pharmaceutical composition comprising an effective amount of one or more compounds selected from isohumolone, isocohumolone, and isoadhumulone of the instant claim 7 (Genus A). See abstract; column 2, structures (IV) to (VI); column 8, claim 1-4.

Tobe does not expressly teach the ratio of the two compounds as about 10:1 to about 1:10 in the composition.

It would have been obvious to a person of ordinary skill in the art at the time of invention to optimize parameters such as effective amounts of the 10:1 to 1:10, to obtain a desired effect.

Claims 1-7 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 5-6 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: Claims 5-6 should depend on Claim 4, and not Claim 1 as recited.